

CLAIMS

What is claimed is:

1. A method of manufacturing a drug eluting implantable medical device, comprising exposing a dry coating on the device to a temperature greater
5 than ambient temperature for a duration of time, the dry coating comprising a polymer, an active agent, and less than about 2% residual fluid content (w/w), wherein the duration of exposure is sufficient to decrease the release rate of the active agent from the coating after the coating has been implanted into a biological lumen.
- 10 2. The method of Claim 1, wherein the dry coating comprises a reservoir layer having the active agent, and a primer layer disposed under a portion of the reservoir layer.
3. The method of Claim 1, wherein the dry coating comprises a reservoir layer having the active agent, and a barrier layer covering a portion of the
15 reservoir layer.
4. The method of Claim 1, wherein the device is a stent.
5. The method of Claim 1, further comprising forming a barrier layer over the dry coating subsequent to exposing the dry coating to the temperature.
6. The method of Claim 1, wherein the active agent is of a type that
20 does not adversely degrade when exposed to the temperature.
7. The method of Claim 1, wherein the act of exposing does not reduce the total content of the active agent in the coating.

8. The method of Claim 1, wherein the polymer comprises an ethylene vinyl alcohol copolymer, an ethylene-vinyl acetate copolymer, poly(butylmethacrylate), or a combination of the same.
9. The method of Claim 1, wherein the act of exposing comprises
5 directing a stream of gas set at the temperature at the coating.
10. The method of Claim 1, wherein the standard deviation of the mean release rate of the active agent in a 24 hour period is lower than the standard deviation of the mean release rate for a group of devices which have not been exposed to the temperature.
- 10 11. The method of Claim 1, wherein the dry coating comprises less than about 1% residual fluid content (w/w).
12. The method of Claim 1, wherein the active agent is rapamycin, 40-O-(2-hydroxy)ethyl-rapamycin, or a functional analog or structural derivative thereof.
- 15 13. A method of manufacturing a stent coating, comprising:
applying a composition to a stent, the composition including a polymer and a solvent;
allowing the solvent to evaporate to form a coating; and
exposing the coating to a temperature equal to or greater than the glass
20 transition temperature of the polymer for a duration of time.
14. The method of Claim 13, wherein the composition further includes an active agent.

15. The method of Claim 14, further comprising forming a primer layer on the stent prior to applying the composition to the stent.
16. The method of Claim 14, further comprising forming a barrier layer over the coating prior to exposing the coating to the temperature.
- 5 17. The method of Claim 14, further comprising forming a barrier layer over the coating subsequent to exposing the coating to the temperature.
18. The method of Claim 14, wherein the active agent is of a type that does not adversely degrade when exposed to the temperature.
19. The method of Claim 14, wherein the act of exposing does not
10 reduce the total content of the active agent in the coating.
20. The method of Claim 14, wherein the active agent is rapamycin, 40-O-(2-hydroxy)ethyl-rapamycin, or a functional analog or structural derivative thereof.
21. The method of Claim 13, wherein the solvent is allowed to
15 evaporate to form a dry coating comprising less than about 2% residual fluid content (w/w).
22. The method of Claim 21, wherein the dry coating comprises less than about 1% residual fluid content (w/w).
23. The method of Claim 13, wherein the temperature is below the
20 melting temperature of the polymer.
24. The method of Claim 13, wherein the composition additionally includes an additive for shifting the glass transition temperature or the melting temperature of the polymer to a temperature different than the actual glass

transition temperature or the melting temperature of the polymer without the additive.

25. The method of Claim 13, wherein the polymer comprises an ethylene vinyl alcohol copolymer, an ethylene-vinyl acetate copolymer,
5 poly(butylmethacrylate), or a combination of the same.

26. The method of Claim 13, wherein the temperature is equal to the glass transition temperature of the polymer plus the melting temperature of the polymer, divided by 2.

27. The method of Claim 13, wherein the temperature is equal to 0.9
10 times the melting temperature of the polymer, wherein the melting temperature of the polymer is expressed in Kelvin.

28. The method of Claim 13, wherein the glass transition temperature is determined by a method selected from the group consisting of dilatometry, differential thermal analysis, differential scanning calorimetry, brillouin light
15 scattering, local thermal analysis, ellipsometry and x-ray reflectivity.

29. The method of Claim 13, wherein the polymer is a blend of two or more polymers.

30. The method of Claim 13, wherein the polymer is a semicrystalline polymer having about 40 to 75 percent crystallinity prior to the act of exposing.

20 31. The method of Claim 13, wherein the polymer is an amorphous polymer.

32. The method of Claim 13, wherein the polymer is a block copolymer.

33. The method of Claim 13, wherein the polymer is a graft copolymer.

34. The method of Claim 13, wherein the polymer exhibits two or more glass transition temperatures, and wherein the method includes exposing the polymer to a temperature equal to or greater than the lowest exhibited glass transition temperature.

5 35. The method of Claim 13, wherein the polymer exhibits two or more glass transition temperatures, and wherein the method includes exposing the polymer to a temperature equal to or greater than the highest exhibited glass transition temperature.

36. A method of manufacturing a drug eluting stent, comprising:
10 applying a composition to a stent, the composition including a semicrystalline polymer, an active agent and a solvent;
allowing the solvent to evaporate to form a dry coating, the dry coating comprising less than about 2% residual fluid content (w/w); and
exposing the dry coating to the crystallization temperature of the polymer
15 for a duration of time.

37. The method of Claim 36, wherein the polymer comprises an ethylene vinyl alcohol copolymer.

38. The method of Claim 36, wherein the active agent is rapamycin, 40-O-(2-hydroxy)ethyl-rapamycin, or a functional analog or structural derivative
20 thereof.

39. A method of manufacturing a drug eluting stent, comprising:
forming a dry polymeric coating on a stent having less than about 2% residual fluid content (w/w), the dry polymeric coating comprising a reservoir layer

including a polymer and an active agent, and a barrier layer including a polymer covering a portion of the reservoir layer; and

exposing the polymer included in the barrier layer to a temperature equal to or greater than the glass transition of the polymer.

5 40. The method of Claim 39, wherein the polymer included in the barrier layer comprises an ethylene vinyl alcohol copolymer, an ethylene-vinyl acetate copolymer, poly(butylmethacrylate), or a combination of the same.

 41. The method of Claim 39, wherein the active agent is rapamycin, 40-O-(2-hydroxy)ethyl-rapamycin, or a functional analog or structural derivative
10 thereof.

 42. The method of Claim 39, wherein the glass transition temperature of the polymer included in the barrier layer is greater than the glass transition temperature of the polymer included in the reservoir layer.

 43. The method of Claim 39, wherein the glass transition temperature of
15 the polymer included in the barrier layer is lower than the glass transition temperature of the polymer included in the reservoir layer.

 44. The method of Claim 39, wherein the glass transition temperature of the polymer included in the barrier layer is about the same as the glass transition temperature of the polymer included in the reservoir layer.

20 45. The method of Claim 39, wherein the temperature is less than the melting temperature of the polymer included in the barrier layer.

 46. The method of Claim 39, wherein the temperature is less than the melting temperature of the polymer included in the reservoir layer.

47. The method of Claim 39, wherein the temperature is equal to the glass transition temperature of the polymer included in the barrier layer plus the melting temperature of the polymer included in the barrier layer, divided by 2.

48. The method of Claim 39, wherein the temperature is equal to 0.9
5 times the melting temperature of the polymer included in the barrier layer, wherein the melting temperature of the polymer included in the barrier layer is expressed in Kelvin.

49. A method of manufacturing a drug eluting stent, comprising:
forming a polymeric coating on a stent, the polymeric coating comprising a
10 reservoir layer including a semicrystalline polymer and an active agent; and
exposing the polymer included in the reservoir layer to the crystallization temperature of the polymer.

50. The method of Claim 49, wherein the polymer comprises an ethylene vinyl alcohol copolymer.

15 51. The method of Claim 49, wherein the active agent is rapamycin, 40-O-(2-hydroxy)ethyl-rapamycin, or a functional analog or structural derivative thereof.

52. A method of manufacturing a drug eluting stent, comprising:
forming a polymeric coating on a stent, the polymeric coating comprising a
20 reservoir layer including a polymer and an active agent, and a barrier layer
including a semicrystalline polymer covering a portion of the reservoir layer; and
exposing the polymer included in the barrier layer to the crystallization temperature of the polymer.

53. The method of Claim 52, wherein the polymeric coating comprises less than about 2% residual fluid content (w/w).

54. The method of Claim 52, wherein the polymer comprises an ethylene vinyl alcohol copolymer.

5 55. The method of Claim 52, wherein the active agent is rapamycin, 40-O-(2-hydroxy)ethyl-rapamycin, or a functional analog or structural derivative thereof.

56. The method of Claim 52, wherein the polymer included in the reservoir layer is a semicrystalline polymer and wherein the crystallization
10 temperature of the polymer included in the barrier layer is greater than the crystallization temperature of the polymer included in the reservoir layer.

57. The method of Claim 52 wherein the polymer included in the reservoir layer is a semicrystalline polymer and wherein the crystallization temperature of the polymer included in the barrier layer is less than the
15 crystallization temperature of the polymer included in the reservoir layer.

58. The method of Claim 52, wherein the polymer included in the reservoir layer is a semicrystalline polymer and wherein the crystallization temperature of the polymer included in the barrier layer is equal to the crystallization temperature of the polymer included in the reservoir layer.

20 59. A method of manufacturing a stent coating, comprising:
applying a composition to a stent, the composition including a polymer and a solvent;
allowing the solvent to evaporate to form a coating; and

exposing the coating to a temperature sufficient to increase the crystallinity of the polymer in at least a portion of the coating.

60. The method of Claim 59, wherein the coating comprises less than about 2% residual fluid content (w/w).

5 61. The method of Claim 59, wherein the composition further includes an active agent.

62. The method of Claim 61, wherein the active agent is rapamycin, 40-O-(2-hydroxy)ethyl-rapamycin, or a functional analog or structural derivative thereof.

10 63. The method of Claim 59, wherein the polymer comprises an ethylene vinyl alcohol copolymer.

64. A method of manufacturing a drug eluting stent, comprising:
forming a polymeric coating including an active agent on a stent strut, the coating having a first segment and a second segment as measured along the length
15 of the stent; and

exposing the first and second segments to different thermal conditions such that the active agent has a higher diffusion rate through the polymer in the first segment of the coating as compared to the polymer in the second segment of the coating.

20 65. The method of Claim 64, wherein the coating comprises less than about 2% residual fluid content (w/w).

66. The method of Claim 64, wherein the polymer comprises an ethylene vinyl alcohol copolymer, an ethylene-vinyl acetate copolymer, poly(butylmethacrylate), or a combination of the same.

67. The method of Claim 64, wherein the active agent is rapamycin, 40-O-(2-hydroxy)ethyl-rapamycin, or a functional analog or structural derivative thereof.

68. The method of Claim 64, wherein the polymer of the second segment is exposed to a higher temperature than the polymer of the first segment.

69. The method of Claim 64, wherein polymeric coating is exposed to a temperature greater than ambient temperature and the polymer of the second segment of the coating is exposed to the temperature for a longer duration than the polymer of the first segment.

70. A stent comprising a radially expandable body and a coating covering at least a portion of the body, the coating comprising a polymer and an active agent, wherein the polymer includes at least two degrees of crystallinity.

71. The stent of Claim 70, wherein the degree of crystallinity is lesser closer to the surface of the stent.

72. The stent of Claim 70, wherein the degree of crystallinity decreases from a shallow region of the coating to a deeper region of the coating.

73. The method of Claim 70, wherein the polymer comprises an ethylene vinyl alcohol copolymer.

74. The method of Claim 70, wherein the active agent is rapamycin, 40-O-(2-hydroxy)ethyl-rapamycin, or a functional analog or structural derivative thereof.

75. A method of coating an implantable medical device, comprising:
5 applying a composition to an implantable medical device, the composition comprising a polymer dissolved in a solvent; and
heating the composition to a temperature equal to or greater than the glass transition temperature of the polymer.

76. The method of Claim 75, wherein the composition is heated to the
10 temperature until a dry coating is formed on the device, the coating comprising less than about 2% residual solvent (w/w).

77. The method of Claim 75, wherein the composition is heated to the temperature until a dry coating is formed on the device, the coating comprising less than about 2% residual solvent (w/w), and for a duration after the dry coating has
15 been formed.

78. The method of Claim 75, wherein the device comprises a metallic body, and wherein the composition is applied to the metallic surface of the body.

79. The method of Claim 75, wherein the composition is substantially free of any active agents.

80. The method of Claim 75, wherein the composition further
20 comprises an active agent.

81. The method of Claim 80, wherein the active agent is rapamycin, 40-O-(2-hydroxy)ethyl-rapamycin, or a functional analog or structural derivative thereof.

82. The method of Claim 75, wherein the polymer comprises an
5 ethylene vinyl alcohol copolymer, an ethylene-vinyl acetate copolymer, poly(butylmethacrylate), or a combination of the same.